

## REMARKS

### **I. Status of the Claims**

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-103, and 108-114 were pending at the time the Office Action dated June 21, 2011 ("the Action") was mailed.<sup>1</sup> Claims 88, 91, 92, 96, 97, and 99 are canceled. Claims 75, 78, 82, 89, 98, 100, 101, 113, and 114 are amended, as described herein. Claims 115-118 are new, as described herein. No new matter is added by the amendments. Following entry of the amendments, claims 75, 76, 78, 80, 82, 83, 89, 93-95, 98, 100-103, and 108-118 are pending.

### **II. The Indefiniteness Rejection Is Overcome**

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-103, and 108-114 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. In particular, the Examiner contends that the term "unsubstituted heteroaryl" is indefinite as there is allegedly "insufficient antecedent basis for this limitation because in formula (II) A2 is substituted with -Y and CR1R2." Action, page 2. Applicants disagree with the rejection because in the chemical arts, use of the word "unsubstituted" in the context of these claims is understood to mean that the heteroaryl is unsubstituted at positions *other than* where the heteroaryl is connected to the rest of the molecule. However, in order to advance prosecution in this case, the term "unsubstituted" is deleted from the A<sub>2</sub> heteroaryl definitions as well as in other claims (e.g., claim 114). Withdrawal of the rejection is respectfully requested.

### **III. The Enablement Rejection Is Overcome**

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-103, and 108-114 are rejected under 35 U.S.C. § 112, first paragraph, as failing the enablement requirement. Although applicants respectfully

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<sup>1</sup> Applicants note that on page 1 of the Action, Claim 79 was indicated as pending. This claim was canceled in applicants' Response filed March 12, 2007.

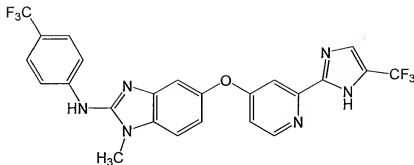
disagree, the independent claims are amended and applicants submit that the amended claims are enabled. Relevant dependent claims are either canceled or amended to align with amendments made to the independent claims, such as regarding A<sub>1</sub>, A<sub>2</sub>, R<sub>1</sub>, R<sub>2</sub>, and R<sub>4</sub>. In addition, to other amendments to claim 113, this claim is also amended to remove redundancies within the claim.

If the Examiner continues to disagree with the claim scope of the independent claims regarding the compound genus, applicants note, in particular, that new claims 115-118 recite more specific substituent combinations. Further comments regarding the new claims are provided below.

Turning to evidence of compounds actually inhibiting Raf kinase activity in a human or animal, applicants reiterate the arguments presented in the Response dated January 11, 2010, on this point, particularly with respect to the fact that breadth of structural diversity does not necessarily equal unpredictability. Although applicants do agree that as between two compounds having different A<sub>1</sub>, A<sub>2</sub>, R<sub>1</sub>/R<sub>2</sub>, and R<sub>4</sub> groups, those two compounds may have different activities, such a difference does not amount to a legal showing of the failure of the enablement requirement. This is especially true in light of the fact that compounds of Examples 1-1054 exhibit an IC<sub>50</sub> with respect to Raf kinase activity of less than 5  $\mu$ m. Specification, page 309, lines 14-15.

Applicants also respectfully reiterate the comments presented in the Response dated July 30, 2009, wherein applicants noted the *in vivo* data pertaining to a compound discussed in U.S. Patent No. 7,482,367 ("the '367 compound"):

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This compound was shown to cause significant tumor growth inhibition or tumor regression in mice xenograft models of melanoma, colorectal carcinoma, and leukemia tumors. The '367 compound falls within the compound genus of the presently amended claims and shows substantial structural similarity to the claimed genus. Applicants submit that this *in vivo* evidence further demonstrates that the claims are enabled.

In view of the foregoing, applicants respectfully request that the enablement rejection be withdrawn.

#### IV. The Double Patenting Rejection Is Overcome

Claims 75, 76, 78, 80, 82, 83, 88, 89, 91-106, and 108-112 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 43-45 of U.S. Application No. 12/315,779 ("the '779 application"). Applicants note that the '779 application has issued into U.S. Patent No. 7,732,465 ("the '465 patent"), which the Examiner cites in a separate rejection. Without conceding the propriety of the rejection, applicants submit a Terminal Disclaimer over the '465 patent. The Terminal Disclaimer is proper as it is accompanied by a Statement Under 37 C.F.R. § 3.73(b). Withdrawal of the rejection is respectfully requested.

#### V. New Claims 115-118 Are Patentable

New claims 115-118 recite a variety of more specific substituent definitions, summarized as follows: a further definition of A<sub>1</sub> of claim 114, based on the recitation of claim 93 (claim

115); an independent claim reciting a combination of further definitions of  $A_1$ ,  $A_2$ , and  $R_1/R_2$ , based on the recitations of claims 92, 98, and 100, respectively (claim 116); a further definition of claim 116's  $A_1$  (claim 117); and a further definition of Claim 117's  $A_1$ , based on the recitation of claim 93 (claim 118). Applicants submit that these claims are enabled. In particular, applicants note that Examples 953-966, 1151, and 1152, are supportive of the  $R_1/R_2$  recitations of the amended claims.

#### **VI. Information Disclosure Statement Acknowledgement**

Applicants filed an Information Disclosure Statement on January 12, 2011, but this IDS was not acknowledged in the present Action. This submitted IDS appears on PAIR. Recognition of the IDS is respectfully requested.

#### CONCLUSION

In view of the foregoing, it is respectfully submitted that each of the pending claims is in condition for allowance, and a Notice of Allowance is requested. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1649.

Respectfully submitted,

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